COVID-19 Response: The case for Phytomedicines in Africa with particular focus on Cameroon*

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Abstract

Despite enormous efforts deployed and considerable positive results obtained in the global fight against the Coronavirus disease 2019 (COVID-19) the scourge remains a major international public health hazard. The main control measures at the onset consisted in the application of barrier and hygiene measures to stop the spread of the virus and case identification and clinical management of symptoms in the absence of widely available anti-COVOD-19 drugs. Vaccination as a major control measure became widely available in the advanced countries of the global north, but not in Africa where less than 5-10% 0f the population are vaccinated against COVID-19. However, African countries, possibly excluding South Africa, have been less impacted by COVID-19 pandemic as they registered fewer cases, hospitalizations and deaths.

Herein it is postulated that the wide use of African traditional Phytomedicines (herbal medicines) has contributed, at least in part, to the better control of the COVID-19 pandemic in Africa. Abundant evidence in the literature suggests the availability of anti-viral, anti-oxidant and immune-stimulatory agents in the proposed COVID-19 herbal remedies., these activities being similar to those the standard drugs used in the standard treatment/ management of COVID-19.

The review also examines a number of COVID-19 herbal medicines including COVID Organics CVO (Madagascar) ADSAR, ELISIR COVID, COROCUR (Cameroon) IHP Detox Tea (Nigeria) and COVIDEX (Uganda) and notes that though approved by the competent authorities in the respective African countries, these phytomedicines have not been approved by the WHO. It is proposed that additional studies be carried out to validate the Africa herbal remedies for possible use as stand-alone or complementary treatment of COVID-19 in addition to vaccination and barrier and hygiene control measures.

Keywords: COVID-19, Phytomedicine, African Traditional medicine, Covid Organics CVO, ADSAR, ELISIR COVID, COROCUR, IHP Tea Detox, STAR YELLOW

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Résumé**

Malgré d'énormes efforts déployés et des résultats positifs considérables obtenus dans la lutte mondiale contre la maladie à Coronavirus 2019 (COVID-19) le fléau reste un danger majeur de santé publique internationale. Les principales mesures de contrôle au début consistaient en l'application de mesures barrières et d'hygiène pour arrêter la propagation du virus et l'identification des cas et la gestion clinique des symptômes en l'absence de médicaments anti-COVOD-19 largement disponibles. La vaccination en tant que mesure de contrôle majeure est devenue largement disponible dans les pays avancés du nord du monde, mais pas en Afrique où moins de 5 à 10 % de la population est vaccinée contre le COVID-19. Cependant, les pays africains, à l'exception peut-être de l'Afrique du Sud, ont été moins touchés par la pandémie de COVID-19 car ils ont enregistré moins de cas, d'hospitalisations et de décès.

Ici, il est postulé que la large utilisation des phytomédicaments traditionnels africains (médicaments à base de plantes) a contribué, au moins en partie, à un meilleur contrôle de la pandémie de COVID-19 en Afrique. De nombreuses preuves dans la littérature suggèrent que la disponibilité d'agents antiviraux, antioxydants et immunostimulants dans les remèdes à base de plantes COVID-19 proposés., ces activités étant similaires à celles des médicaments standard utilisés dans le traitement/la gestion standard de COVID- 19.

L'article examine également un certain nombre de médicaments à base de plantes COVID-19, notamment COVID Organics CVO (Madagascar) ADSAR, ELISIR COVID, COROCUR (Cameroun) IHP Detox Tea (Nigeria) et COVIDEX (Ouganda) et note que, bien qu'approuvés par les autorités compétentes dans le pays africains respectifs, ces phytomédicaments n'ont pas été approuvés par l'OMS. Il est proposé que des études supplémentaires soient menées pour valider les remèdes à base de plantes d'Afrique pour une utilisation possible comme traitement autonome ou complémentaire de COVID-19 en plus de la vaccination et des mesures de barrière et de contrôle d'hygiène.

Mots clés : COVID-19, Phytomécine, Médecine traditionnelle africaine, Covid Organics CVO, ADSAR, ELISIR COVID, COROCUR, IHP Tea Detox, STAR YELLOW C

**(The abstract was translated from English to French translated by Google Translator and revised by the Author)

INTRODUCTION

The Corona Virus Disease 2019 (COVID-19) caused by the Severe Respiratory Syndrome Virus-2 (SARS-CoV-2) that erupted in Wuhan China in December 2019 rapidly spread around the world causing suffering and death as well as disrupting lifestyles and economies. Currently on 7th October 2021 the dismal statistics of COVID-19 pandemic stands at 237,693,189 million cases and 4,852,326 deaths world-wide. Compared to the global North the impact of COVID-19 has been relatively less severe in Africa although the number of cases and deaths are rising in Africa as well. For, example the number of cases and deaths in Cameroon have nearly doubled over the past twelve months and now stand at 95,399 cases and 1,517deaths respectively (www.worldometers.info accessed 07/10/2021).

The current control measures recommended by the WHO and adopted by many countries around the world are two pronged: a) barrier and hygiene measures to stop the transmission such as social distancing, hand washing, wearing of face masks, lockdowns and self-isolations etc b) case identification and management for those who develop symptoms and require hospitalization. Although therapies like monoclonal antibodies, remdesivir, baricitinib, have been introduced with varying degrees of success in the developed world these drugs are either too expensive or not easily available to most African countries. As for the barrier-measures they were respected initially, but have subsequently been abandoned by a majority of the African population though officials can still be spotted on TV wearing masks and doing fist bumps, more because it is government policy rather than because of its usefulness to fight the pandemic.

Despite predictions of massive deaths in Africa as a result of COVID-19 the continent has generally continued to resist the pandemic better than the rich northern countries where the disease first erupted (www.worldometers.info ; Laurencin Mc Clinton,2020). Rather than celebrate that we in Africa have so far not been hardly hit by the current variants of the virus, we urgently need to learn from any good practices we have developed so far and consolidate them going forward.

Researchers have cited the relatively young population of Arica as compared to the global north, in-built genetic factors, the abundance of sun-light induced vitamin D and many other factors to explain the resilience of the African population against the virus (Marsh and Alobo, 2020) However, Africans and people of African descent in Europe and the Americas have suffered disproportionately higher death rates from COVID-19 than their counterparts in Africa, casting doubts on any intrinsic resistance capacity of Africans (Laurencin & McClinton, 2020).

The global strategy for the fight against COVID-19 has been almost exclusively based on evidence-based Allopathic (Western) Medicine practice, almost to the exclusion of African traditional medicine. The main symptoms of COVID-19 include fever, cough and body pains that occur frequently and half a dozen other less frequent symptoms (www.cdc.gov; www.who.int) In sub-Saharan Africa fever and the other flu-like symptoms are often treated with medicinal herbs regardless of their etiologies. It is hereby proposed that the wide use of African traditional herbal medicine has both prophylactic and curative impact on COVID-19 in sub-Saharan Africa. The aim of the present article is to present supportive evidence from the literature for this hypothesis and propose a way forward to integrate traditional African herbal medicine into the fight against COVID-19 and other pandemics.

METHODOLOGY

Literature search

The databases www.scholar.google.com and www.yahoo.com were searched for scholarly articles using the following key words:

COVID-19 drug targets; COVID-19 anti-viral compound from medicinal plants;

Phytomedicine for COVID-19, fever, cough, body pains;

African traditional medicines for COVID-19, fever, cough, body pains

The databases www.cdc.gov ; www.who.int; www.worldometers.info were consulted for statistical information about COVID-19, its pathogenesis, treatment and prevention.

Hypothesis and Research Design

Traditional African medicine approach for the diagnosis of diseases is heavily dependent on symptoms with very little or no laboratory tests to confirm the diagnosis. In the case of COVID-19 the most prevalent symptom is fever. Fever in tropical Africa is mostly caused by malaria parasites (Plasmodium falciparum mostly). Bacteria, rickettsia, viral infections including HIV/AIDS also cause fevers in this milieu. Thus, it was hypothesized that herbal medicines frequently used to treat malaria and other fevers are likely to be effective against COVID-19 as well.

To verify this hypothesis, firstly, we checked in the literature whether the plants used for the treatment of fevers also contained anti-viral compounds and could also act against some of the symptoms of COVID-19.

Secondly, we reviewed the phytomedicines reported in the social media and the scientific literature as to whether they had been properly validated by well-structured ,randomized, controlled clinical trials.

Finally, we highlighted the need for randomized controlled trials to validate the safety and efficacy of traditional herbal medicines before they are authorized for general use.

RESULTS

Why Phytomedicines?

Plants are known to be rich sources of bioactive compounds that have been developed into patent medicines (Titanji et al 2007; Helmestine ,2020). A large body of evidence confirms the availability of antiviral compounds isolated from the medicinal plants of Africa and China.(Muhtara et al, 2008;Asprilio and Wilar,2021,) Phytomedicines are used by more than 80% of the African population because of their availability and affordability. There is laboratory evidence that plant products are active against other enveloped virus like HIV-1 and HIV 2 and may be active against the COVID-19 virus as well.

Since the outbreak of COVID-19 many reports in newspapers and social media have touted various herbal preparations as cures for the disease. These need to be tested for safety and efficacy to avoid unwanted side effects. The route to the preparation of improved traditional medicines is considerably shorter than that for allopathic medicines, since most herbal medicines have been used by the population over the years apparently safely. Besides Phytomedicines usually contain multiple active principles and are thus less likely to induce resistance in contrast to single component drugs against which resistance can easily be developed.

Overview of antiviral products from African medicinal plants.

There are over 68000 plant species in Africa of which 35000 are thought to have originated from other continents. Recent reviews by Sohail et al (2020), Akindele et al (2020) Oladele et al
Attah et al (2021) Nair et al (2021) Asprilio and Wilar(2021) suggest the occurrence of antiviral agents in a wide variety of plants. Some of the identified antiviral agents are active against COVID-19 symptoms, while others have been shown to inhibit the COVID-19 virus in vitro. So far most of the plant antiviral agents have been tested in vitro on cell lines, but not yet in clinical trials. Consequently, their usefulness as anti-COVID drugs remains to be determined.

General mechanisms of Anti-Infective drug Action.

Anti-infective drugs can be deemed to fall into two broad groups:

1. Direct-acting drugs. These bind to and inhibit or block the functioning of the pathogen (bacteria, fungi, parasite, virus etc.) thereby eliminating the pathogen.

2. Indirect-Acting drugs. These perform by:

   -Alleviating/reversing the symptoms provoked by the pathogen like inflammation, mechanical damage and or stimulating the immune system to fight against the invading pathogen.

The theoretical possibility for a drug to belong to both groups is not excluded although it is not discussed subsequently herein.

Modes of Action of anti-COVID drug candidates.

Over a hundred drug candidates are currently being tested for the treatment of COVID-19 (www.fda.gov) and can be classified into the same groups as described above.

1. Direct acting drugs. These include growth and replication inhibitors; RNA dependent DNA polymerase inhibitors; Angiotensin-Processing Enzyme inhibitors; Protease inhibitors PRO; CLO Pro).

2. Indirect Acting drugs:

   -anti-inflammatory agents

   -anti-oxidants

   -Immuno-modulatory agents

   -anti COVID symptoms (fever, cough, body pains, loss of tase, loss of appetite etc.)

Table 1 gives examples of anti-COVID drugs in current use grouped into the Direct and Indirect-Acting Groups. It can be seen that the vast majority of currently approved treatments fall in the indirect-acting group.

Table1: Selected drugs sed for COVID-19 treatment/management

Drug Type	Examples	Comments
Direct Acting (causative)	Monoclonal antibodies (Mabs): bamlanivimab; etesevimab; **	Several have been developed and authorized. Mabs act by binding to a neutralizing the virus
	Remdesivir	Blocks viral replication by inhibiting the RNA dependent RNA Polymerase of the coronavirus*
	molnupiravir	Interferes with corona virus replication*; approved in the UK and under review in several other countries including the EU and USA.
Indirect Acting (symptomatic)	baricitinib	Disrupts inflammation by blocking JAK1 and JAK2 protein kinases. *
	dexamethasone	Broad spectrum anti-inflammatory steroid to be used under medical supervision
	Vitamin C	Broad spectrum Anti-oxidant***
	Vitamin D3	Immunomodulator***

Sources: *https://go.drugbank.com accessed 05/11/2021 **www.who.int accessed 25/10/2021 ***Recommended by Cameroon Ministry of Health for the management of mild COVID-19 cases alongside other treatments.

A recent survey by Fedoung et al (2021) reported on the statistics of plants with anti-COVID activities. Of the 230 species reviewed for the fight against the COVID-19, 30 were reported to contain confirmed anti-covid-19 secondary metabolites directly acting on the virus; 90 plant species were used to manage at least three of the common symptoms of COVID-19; 10 were claimed to have immunostimulant activity; 52 were reported to have anti-inflammatory; 14 had anti-viral properties distinct from COVID-19; while as many as 78 species were reputed to have documented anti-malarial activities. Impressive as these findings are, they need to be read with caution: the methods used for demonstrating anti-viral activities were not standardized; in-vitro activities often do not predict what would happen in-vivo in the human host; the toxicity and safety of the products were not reported; and finally, there is some redundancy as some plants may display more than one activity. This review highlights the necessity to explore in greater detail especially those plants which are currently used in traditional herbal medicines against COVID-19.

Selected examples of Plants with anti-Covid-19 products from medicinal plants.

a) A number of **Direct-Acting** plant extracts have been reported. It has been shown that extracts of *Nigella sativa* inhibit SARS CoV-2 replication in vitro (). This is interesting because the seeds of this plant are used as a spice and for medicinal purposes.

Artemisia annua extracts were shown to inhibit SARS-CoV-2 replication in vitro, but the inhibition was not caused by artemisinin or its derivatives. Artemisinin is a well-known antimalarial drug (Nie et al, 2021)

Extracts of *Borreira verticillata* also showed anti-viral effect on velo E6 cells. Large scale screening showed that two natural products from African medicinal plants, Corilagin and rhoifolin were able to inhibit SRARS-CoV-2 replication in vitro with IC_{50} values in the micromolar range. Corrilagin is found in plants of the Euphorbiaceae eg *Acalypha wikesiana* Muel*; Acalypha australis*, Euphorbia longana Lamet. Rhoifolin is a tri-substituted flavone found in *Uraria picta*.

development of these products into anti COVID drugs will require not only a demonstration of safety and efficacy in animal models and non-human primates, but also strategies to scale up the production of the compounds (Attah et al,2020) This is time consuming and capital intensive like any other drug development process following the classical route. In the meantime, many common medicinal plants are being repurposed for the treatment of COVID1-19 as discussed in the next section.

Plants used for the treatment of malaria and other fevers 'repurposed' for the treatment of COVID-19.

Table 2 gives a number of plants frequently cited in the reviewed literature and by traditional medicine practitioners to prepare broths, infusions and steam baths for the treatment of COVID-19. The plants are cited in alphabetical order and no indication of how they are harvested, preserved, prepared or used is either implied or recommended. Interested users should contact a qualified healthcare giver for advice. On table 2 are also indicated some of the activities that may be relevant for the symptomatic treatment of COVID-19.

Table 2: Selected plants used for the treatment of fevers and malaria repurposed for the treatment of COVID-19 symptoms

Scientific name	**Common Name**	**Parts used**	**Antiviral**	**Anti-malarial**	**Anti-Oxidant**	**Anti-Inflammatory**	**Immuno-modulatory**
Allium sativum	garlic	bulb	+	ND	+		+
Bides pilosa	Black Jack	leaves		+			
Carica papaya	Pawpaw	leaves		+			
Cinchona		Stem bark		+			+
Cinnamomum zeylanicum	cinnamon						+
Citratus aurantium	Lime	fruit					
Curcuma longa	turmeric					+	
Cymbopogom citratus	Fever grass	leaves		+			
Garcinia cola	Bitter cola	fruit					
Mangifera indicus	Mango	leaves					
Moringer oleifera	leaves				+		
Musa paradaica	fruits				+		
Psidium guajava	Guava	leaves	+				
Vernona amygdalina	Bitter leaf	leaves			+		+
Zengiber officinale	Ginger	rhizome		+			+

ND of Blanks = Not determined; + menas activity present

CASE STUDIES

In the following section a number of African herbal medicines, which have made headlines in the social media and other press organs will be presented as case studies.

CASE STUDY-1

1. Name of Phytomedicine: Covid organics (CVO)
2. Promoter/Inventor: Institut Malagashe de Recherches Appliquees, IRMA
3. Country of origin: Madagascar
4. Plants used: *Artemesia annua and* other undisclosed plants
5. Presentation: In liquid form
6. Indications for Use: Proposed for treatment of COVID-19
7. Has Authorization been granted? Yes, Madagascar has approved the Phytomedicine but not the WHO

8. Sources of Information: Press releases; https://en.m.org accessed 18/9/2021

9. Has Phytomedicine undergone randomized controlled clinical trials? No

10. Comments: Uncontrolled clinical observations have been reported. Madagascar is reported to be testing the drug in collaboration with the WHO. Results are still awaited.

CASE STUDY-2

1. Names of Phytomedicine: ELISIR COVID; ADSAK
2. Promoter/Inventor: Bishop Samuel Klader
3. Country of origin: Cameroon
4. Plants used: Not disclosed
5. Presentation: In liquid form
6. Indications for Use: Adjuvant for the treatment of COVID-19
7. Has Authorization been granted? Yes, by the Ministry of Public Health of Cameroon
8. Sources of Information: Ministerial letter circulated in the national press and social media
9. Has Phytomedicine undergone randomized, controlled clinical trials? No
10. Comments: The phytomedicine has been widely distributed in Cameroon. The inventor claims that the Phytomedicines are effective as cures and prophylactics. There are two preparations, ELISIR COVID and ADSAK COVID. No information has been published about their differences and when to use them. With the authorization granted by the Ministry of Public health randomized and controlled trials are indicated to confirm the efficacy and safety of these herbal medicines.

CASE STUDY-3

1. Name of Phytomedicine:COROCUR
2. Promoter/Inventor: Dr Yiagnigni Mfopou Euloge
3. Country of origin:Cameroon
4. Plant used: *Thymos vulgaris*
5. Presentation: Dry powder
6. Indications for Use: Adjuvant treatment of COVID-19
7. Has Authorization been granted? Yes, By the Ministry of Public Health of Cameroon
8. Sources of Information: Authorization letter by Minister of Public Health. https:// ecomnewsafrique.com/2021/07/26 Cameroun. corocur/
9. Has Phytomedicine undergone randomized controlled clinical trials? No
10. Comments: The inventor Dr Yiagnigni is a cardiologist. He stated in an interview that he had treated 1500 patients successfully and had provided a file to the Ministry of Health demonstrating the efficacy and safety of Corocur. No peer reviewed publications on COROCUR have appeared.

CASE STUDY-4

1. Name of Phytomedicine: IHP Tea Detox
2. Promoter/Inventor: Bioresource Development Group (BDG)
3. Country of origin: Nigeria
4. Plants used: *Andrographis panniculata; Garcinia kola and Psidium guajava*
5. Presentation: As a tea
6. Indications for Use: Treatment of COVID 19
7. Has Authorization been granted?: NO
8. Sources of Information: www.pactr.orgno PACTR 202004761408382; Attah et al (2020)
9. Has Phytomedicine undergone Clinical trials? Not approved clinical trials are ongoing.
10. Comments: Several other preparations have been put on the market in Nigeria but have not yet been approved by the Nigerian government agency NAFDAC. These include IHP Garcinia, IHP Immunovit and GUGzin 290 mg by Pax Herbal Nigeria (Attah et al,2020)

CASE STUDY-5

1. Name of Phytomedicine: STAR Yellow
2. Promoter/Inventor: Professor Julius Oben et al (2020)
3. Country of origin: Cameroon
4. Plants used: 10 plants including C.mannii and Allium Sativum
5. Presentation: Presented as a liquid termed Yellow Sauce popularly called Achu soup/sauce in Cameroon
6. Indications for Use: To prevent the transmission of Covid virus through feces
7. Has Authorization been granted? No
8. Sources of Information: *Functional Foods in Health and Disease 2020 vol 10(8): 324-329*
9. Has Phytomedicine undergone a randomized controlled clinical trial? No
10. Comments: The authors have carried out acceptability trials and found Star Yellow to be more acceptable to consumers than the traditional yellow sauce or Achu soup. However, the anti-COVID-19 viral activity claimed by the authors remain to be proven.

CASE STUDY-6

1. Name of Phytomedicine: COVIDEX
2. Promoter/Inventor: Patrick Ogwang
3. Country of origin: Uganda
4. Plants used: Z.gilleti; Warburgia ugandensis and a third undisclosed plant.
5. Presentation: In liquid form in bottles containing 20ml of the herbal medicine.
6. Indications for Use: Treatment of COVID-19 as an adjuvant
7. Has Authorization been granted? Yes, by the Uganda National Drug Authority
8. Sources of Information: Simon Kasyate. The Observer, July 7 2021 (Search www.google.com with key words 'Covidex, Uganda COVID-19 herbal medicine')
9. Has Phytomedicine undergone randomized controlled Clinical trials? No

10. Comments: The inventor revealed in an interview that he had conducted a lot of observational trials and submitted a file to the Uganda National drug authority with efficacy and safety data. The Inventor declared that he had received a strong support from the President Museveni and the Uganda Ministry of Science and Technology. No peer reviewed publication could be found on COVIDEX.

DISCUSSION

The main aim of this paper was to present the case for traditional African herbal medicine as a resource for the fight against the COVID-19 pandemic. To buttress this case, literature sources have been cited and the case studies in which evidence has been presented to indicate the wide use of herbal medicine preparations to manage COVID-19 (cf list of References). The literature demonstrates the occurrence in the medicinal plants of anti-viral compounds as well as anti-oxidants, anti-inflammatory compounds and immunostimulants that have been used in the presumptive management of COVID-19. Since most of the traditional herbal medicines have not been validated in randomized controlled clinical trials, it is difficult to quantify their efficacy and safety. This is not surprising since the approaches of African traditional herbal medicine are different from those of Allopathic medicine (Table 3) . The differences not withstanding it is important that all medicines must fulfill the safety and efficacy requirements before they are authorized for use as stand-alone or complementary treatments. Thus, the WHO has recommended procedures for validation of traditional herbal medicines, which have also been adopted by the African Union Center for Diseases control (WHO,2000 &2006). At least one of these herbal medicines IHP Detox Tea is undergoing clinical trials.

Furthermore, an examination of the overall statistics of the COVID-19 worldwide prevalence shows that, so far, Africa has resisted the spread of the pandemic better than the Global North and South America. Factors such as the relatively younger African population, the availability of sunlight induced vitamin D and even genetic factors are unlikely to explain the difference given the fact that Africans and People of African descent living in Europe and the Americas have been disproportionately more affected than other ethnicities in the same areas. Although direct causal proof of the efficacy of African Traditional herbal medicines for COVID-19 treatment has not yet been presented, there is a lot of indirect supporting evidence. When COVID-Organics from Madagascar was first presented as a cure it became controversial because supporting scientific evidence was lacking. However, it continued to be used. The evolution of the pandemic in Madagascar has been relatively slower than in neighboring South Africa where the COVID-19 response relied almost exclusively on Allopathic Medicine. The same can be said of Bishop Samuel Klader's herbal medicines Elisir and Adsak (Case Study- 2) They were distributed to thousands of people who tested positive for COVID-19 and according to the press release none of the patients progressed to severe disease. An important reservation is that there was no control group which did not receive the herbal treatment. Now that the Elisir and Adsak have been approved as adjuvant or complementary treatments for COVID it is urgently necessary to validate and quantify their efficacy in randomized controlled trials following the WHO protocols (WHO, 2000.)

The development of African traditional herbal medicines against COVID-19 should not be used as a pretext to abandon barrier measures and vaccination as proven control methods. Rather, they should be used in combination to eventually rid the continent of the COVID-19 pandemic.

Table 3. Some important differences between Allopathic and African traditional Medicine

Allopathic medicine	**African Traditional Medicine**
Diagnosis, treatment and prevention are evidence-based	Diagnosis and treatment based on symptoms and signs. Religious and spiritual methods employed (without proof) for diagnosis and treatment
Heavily dependent on and sophisticated equipment	Personnel are trained informally through apprenticeships with no certification and/or licensure
Expensive and thus not easily accessible in low-income settings	Available at affordable prices
Well-structured and regulated with quality assurance envisaged	Mostly informal with no quality assurance measured enforced
Ethical oversight envisaged and backed by laws and regulations	Ethical oversight implicit in local customs but these are crumpling under the weights of urbanization and modernization

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